REMARKS:

At the outset, Applicants wish to thank Examiner Kaushal and Examiner Fredman for graciously acquiescing to and participating in the interview held on June 2, 2004. As agreed among the interview attendees, Applicants present herein new claims, which broaden the scope of the claims by removing unnecessarily limiting language and which are submitted to place the claims in condition for allowance.

Specifically, in this Amendment, claims 1-259 have been cancelled without prejudice or disclaimer. New claims 260-280 are presented herein. The currently-pending claims are now claims 260-280.

The newly-presented claims are supported by the instant application and the previously-filed claims. No new matter has been introduced into the application by virtue of the new claims. Specifically, support for new claim 260, directed to a method comprising the use of an enriched population of skeletal muscle derived myoblasts is found throughout the instant specification, *inter alia*, for example, Fig. 2, Figs. 15A-15C; at page 17, lines 5-11; at page 30, lines 21-25; at page 43, lines 1-2 (enriched population of myoblasts); and at page 61, lines 6-10 and Example 5. Support for new claims 261-273 is found throughout the instant specification as well as in the previous claims. Further support for new claims 267 is found in the declaration of Dr. Chancellor, e.g., Appendix 2, as submitted in this application on January 8, 2004. More specifically, support for new claims 265 and 272 is found in the instant specification, *inter alia*, at page 82, lines 17-28.

Applicants respectfully submit that new claims 274-280 also cover allowable subject matter, based on the contents of new claims 260-273.

In the Remarks below, the Office Action dated January 29, 2004 has been considered as if it pertains to newly presented claims 260-281. Thus, this Amendment is responsive to the January 29, 2004 Office Action as if it applies to the new claims.

I. The Enablement Rejection

Claims 196-259 stand rejected under 35 U.S.C. §112, first paragraph, as the specification allegedly does not enable one skilled in the art ... to make and/or use the invention commensurate in scope with these claims.

In the Office Action, the Examiner comments on the breadth of the claims and the guidance provided in the specification. More particularly, the Examiner opines that the specification "fails to disclose a method of treating stress urinary incontinence by repairing or ameliorating any and all sites in the genitourinary tract tissue by injecting any an all types of undifferentiated muscle derived cells".

In response, Applicants submit that the presently claimed invention, i.e., the introduction of an enriched population of autologous, skeletal muscle-derived myoblasts into urethra and/or sphincter muscle tissue for ameliorating stress urinary incontinence (SUI), is fully supported by the instant specification, as recognized by the Examiner at page 3, paragraph 1, of the 01/29/2004 Office Action. In addition, and as also recognized by the Examiner, the introduction of skeletal muscle-derived myoblasts into urethra and sphincter muscle tissue is clearly associated with the amelioration of SUI. As presently claimed, Applicants' invention is neither unpredictable nor of undue breadth.

It is also respectfully submitted that, contrary to the Examiner's remarks, Applicants have described and used several different models of urethral or sphincter injury associated with SUI to demonstrate the effectiveness of the described skeletal muscle-derived cells, i.e., skeletal muscle-derived myoblasts, for the amelioration of SUI. Specifically for example, in Appendix 1 of the Chancellor declaration submitted with Applicants' January 8, 2004 response, cauterization was used to create urethra injury as a model for intrinsic sphincter deficiency (ISD), which is a recognized cause of one type of SUI. The results of the experimental studies described in Appendix 1 of the Chancellor declaration demonstrated that skeletal muscle-derived myoblast injections restored the mean urethra leak point pressure (LPP) of injured animals to control levels

by 6 weeks post surgery. In a second set of experiments described in Appendix 2 of Dr. Chancellor's declaration, the rat model of urinary incontinence involved urethral denervation. In the experiments in Appendix 2, skeletal muscle-derived myoblasts were injected into sphincter muscle tissue and amelioration of SUI was demonstrated. In both the first and second sets of experiments of the Chancellor declaration, the presence and bulking of the injected cells in muscle tissue over time were monitored by the expression of β-galactosidase in the injected site, as the cells were transduced to contain an exogenous LacZ reporter gene, which was successfully expressed in the cells. (See, e.g., the Chancellor application at page 22, lines 19-27; Figs. 15A-15C; page 46, lines 5-28 to page 47, lines 1-28; and page 65).

Further, in the paper of J.Y. Lee et al. (2003, "The effects of periurethral muscle-derived stem cell injection on leak point pressure in a rat model of stress urinary incontinence", *Int. Urogynecol. J.*, 14:31-37), of record, urethral degeneration induced by sciatic nerve denervation was used as a model of SUI. In experiments employing this model, the cells administered in accordance with the present invention were shown to improve incontinence at 1 and 4 weeks post injury.

In addition, Example 2 of the instant specification describes the injection of skeletal muscle-derived myoblasts into the urethra wall to treat urethra injury in a mouse model system involving cryo-injury or cryo-damage. Example 2 demonstrates that the injected cells survived in this animal model of urethral injury, as evidenced by being monitored for 30 to 60 days following introduction into the animal needing treatment, and allowed the formation of regenerative myofibers in the urethra wall, which is comprised of muscle tissue. Animals that had been treated by injection of these cells exhibited increased urethral pressure. Improved urethral contractility was also described in those animals having injury to the urethra and receiving the injected cells. The instant specification also teaches a urethral obstruction model (Example 1, page 41).

The instant specification also teaches that the injection of rat skeletal muscle-derived myoblasts according to Applicants' method resulted in a large bulking effect in the urethra wall, as shown in Fig. 15C, which depicts the cross section of a rat urethra after treatment with the injected cells. Also, as shown in Figs. 15A, 15B and Example 4, these cells survived for at least 6 months following injection into mouse bladder and urethra without damage to the walls of the muscle tissue, and expression of ß-galactosidase encoded by the LacZ gene transduced into the cells prior to injection was maintained at approximately 66% after 70 days. These results support the ability of the skeletal muscle-derived myoblasts of the invention to persist at the site of injury or damage to genitourinary muscle tissue and to ameliorate stress urinary incontinence.

Accordingly, in view of the present claims and the above remarks, reconsideration and withdrawal of the §112, first paragraph, rejection are respectfully requested.

II. The Indefiniteness Rejection

Claims 196-259 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner has remarked that the term "undifferentiated muscle derived cells (MDCs)" in the relevant claims is a relative term which renders the claim indefinite.

Applicants respectfully submit that the newly presented claims overcome this rejection by reciting 'skeletal muscle-derived myoblasts', which allows one of ordinary skill in the art to reasonably ascertain the scope of the invention as claimed. This language is clearly supported by the instant specification, which describes skeletal muscle-derived myoblasts, as well as a process to obtain an enriched population of these cells. (*See*, e.g., the instant disclosure at page 42. lines 10-28 to page 43, lines 1-2; at page 67, lines15-28 to page 68. lines 1-6; and at page 98, lines 21-28 to page 99, lines 1-10).

Applicants respectfully submit that the present claims describe and define with clarity the subject matter of the invention. Accordingly, reconsideration and withdrawal of the §112, second paragraph rejection are respectfully requested.

CONCLUSION

Applicants respectfully submit that the presently pending claims are in condition for allowance, and an action progressing this application to issue is courteously urged.

Should any fees additional to those paid herewith be deemed to be properly assessable during the pendancy of this application, or for the timely consideration of this Amendment, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. 08-0219, Order No. PIT-010.

If the Examiner is of the opinion that further discussion would be helpful in progressing this application to allowance, he is respectfully requested to telephone the applicant's undersigned representative directly at (212) 937-7315.

Respectfully submitted,

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